Cell Biology

KSR'S ROLE IN THE RAS PATHWAY. Roberta Litavecz, Catherine A. Craft, Guillermo Romero, and Mary K. Ritke. Department of Biology, University of Indianapolis, Indianapolis IN 46227 and Department of Pharmacology, School of Medicine, University of Pittsburgh, Pittsburgh PA 15261. Litaveczra@uindy.edu, mritke@uindy.edu

The Ras pathway, also known as the mitogen-activated protein kinase cascade (MAPK), is important for cell growth and differentiation. In fibroblasts, the Ras pathway studied begins with the stimulation of the cell surface insulin receptor, which then leads to the activation of the G-protein Ras, a peripheral membrane protein. Activated Ras, in a series of phosphorylations, activates the MAP kinase kinase kinase, Raf, which in turn leads to the activation of MEK, and then ERK. Specific experiments were designed to show the role of Kinase Suppressor of Ras (KSR), in the MAP kinase cascade of rat fibroblasts. It has been previously shown in other cell lines that KSR acts as a scaffolding protein, to shuttle specific proteins of the MAP kinase pathway to areas of activation in the cell. It was thus hypothesized that in rat fibroblast cells over-expressing the human insulin receptor (HIRcB cells), KSR would also act in this manner. This hypothesis was tested by immunoprecipitation of KSR, followed by western blot analysis of the immunoprecipitates with antibody to MEK or ERK. Preliminary results indicate that MEK and ERK do form complexes with KSR, and complex formation is increased slightly by insulin treatment. However, preliminary evidence has shown that addition of phosphatidic acid significantly reduces the amount of complexes recovered.